CLAIMS:

~~1. A homo-bivalent linker compound comprising identical functional groups at either end, wherein said functional groups are joined by a linking group comprising at least one amide bond.~~

~~2. The homo-bivalent linker compound of claim 1, wherein the at least one amide bond is a eupeptide bond.~~

~~3. The homo-bivalent linker compound of claim 1, wherein the at least one amide bond is an isopeptide bond.~~

~~4. The homo-bivalent linker compound of claim 1, wherein the at least one amide bond is formed from the joining of two amino acids.~~

~~5. The homo-bivalent linker compound of claim 4, wherein each of the amino acids is independently naturally occuring or non-naturally occuring.~~

~~6. The homo-bivalent linker compound of claim 4, wherein each of the amino acids is independently an alpha, beta, gamma, or delta amino acid.~~

~~7. The homo-bivalent linker compound of claim 4, wherein at least one of the amino acids is an alpha amino acid; or wherein each of the amino acids is an alpha amino acid.~~

~~8. The homo-bivalent linker compound of claim 4, wherein at least one of the amino acids is a proteogenic amino acid; or wherein each of the amino acids is a proteogenic amino acid.~~

~~9. The homo-bivalent linker compound of any of claims 1 to 8, wherein the identical functional groups are maleimide, azide, alkyne, activated carboxyl or amine.~~

~~10.~~1. ~~The~~ A homo-bivalent linker compound ~~of any of claims 1 to 9, wherein the compound~~ comprisinges Structure 1:

(X)-<--->-▢-<--->-(X) (Structure 1)

wherein,

(X) is a function group, optionally (X) is a maleimide, azide, alkyne, activated carboxyl or amine;

each <---> is independently a spacer group, which may be present or absent, optionally, each <---> is independently alkyl, alkoxy, cyclyl, heterocyclyl, aryl, heteroaryl, or substituted versions thereof.; and

▢ is a linking group comprising at least one amide bond, optionally, ▢ comprises 1, 2, 3, or more than 3 amide bonds.

~~11. The homo-bivalent linker compound of claim 10, wherein X is a maleimide, azide, alkyne, activated carboxyl or amine.~~

~~12. The homo-bivalent linker compound of claim 10 or 11, wherein each spacer group <---> that is present in the compound is, independently, alkyl, alkoxy, cyclyl, heterocyclyl, aryl, heteroaryl, or substituted versions thereof.~~

~~13.~~2. The homo-bivalent linker compound of claim ~~12~~1, wherein each spacer group <---> that is present in the compound is, independently, C_{1-10} alkyl, C_{1-10} alkoxy, 5-10 membered aryl, 5-10 membered heteroaryl, 5-10 membered heterocyclyl, (C_{1-10} alkyl)-(5-10 membered aryl), (C_{1-10} alkyl)-(5-10 membered heteroaryl), or (C_{1-10} alkyl)-(5-10 membered heterocyclyl); optionally each spacer group <---> that is present in the compound is, independently, C_2 to C_6 alkyl, ethylene glycol, triethylene glycol, or 1,4-phenylene.

~~14. The homo-bivalent linker compound of claim 13, wherein each spacer group <---> that is present in the compound is, independently, C_2 to C_6 alkyl, ethylene glycol, triethylene glycol, or 1,4-phenylene.~~

~~15. The homo-bivalent linker compound of any of claims 10 to 14, wherein the linking group ▢ comprises 1, 2, 3, or more than 3 amide bonds.~~

~~16.~~3. The homo-bivalent linker compound of claim ~~15~~1, wherein the linking group ▢ comprises 1, 2, or 3 amide bonds; optionally wherein the linking group ▢ comprises at least one amide bond formed from the linkage of two amino acids.

~~17.~~4. The homo-bivalent linker compound of claim ~~16~~3, wherein the linking group ▢ comprises:

(i) one amide bond formed from the linkage of two amino acids;

(ii) two amide bonds formed from the linkage of three amino acids; or

(iii) three amide bonds formed from the linkage of four amino acids.

~~18.~~5. The homo-bivalent linker compound of any of claims ~~10~~ 1 to ~~17~~4, wherein each of the amide bonds is, independently, a eupeptide bond or an isopeptide bond.

~~19.~~6. The homo-bivalent linker compound of any of claims ~~16~~ 3 to ~~18~~5, wherein at least one amino acid is Glycine, Alanine, Proline, Valine, Lysine, Aspartic Acid, Citrulline, and Beta-alanine.

~~20. The homo-bivalent linker compound of any of claims 16 to 19, wherein at least one amino acid is Alanine.~~

~~21. The homo-bivalent linker compound of any of claims 16 to 20, wherein at least one amino acid is Proline.~~

~~22. The homo-bivalent linker compound of any of claims 16 to 21, wherein at least one amino acid is Valine.~~

~~23. The homo-bivalent linker compound of any of claims 16 to 22, wherein at least one amino acid is Lysine.~~

~~24. The homo-bivalent linker compound of any of claims 16 to 23, wherein at least one amino acid is Aspartic Acid.~~

~~25. The homo-bivalent linker compound of any of claims 16 to 24, wherein at least one amino acid is Citrulline.~~

~~26. The homo-bivalent linker compound of any of claims 16 to 25, wherein at least one amino acid is Beta-alanine.~~

~~27.~~7. The homo-bivalent linker compound of any of claims ~~10~~ 1 to ~~26~~6, wherein the linking group ▢ comprises Structure 2:

$$R\text{-}A_a\text{-}B_b\text{-}C_c\text{-}D_d\text{-}R^{1}$$ Structure 2

wherein:

R is H, or is absent;

R^{1} is OH, or is absent;

each of a, b, c, and d is independently 0 or 1, with the proviso that the sum of a + b + c + d is greater than or equal to 2; and

each of A, B, C and D independently comprises Structure 3:

$$[N\blacktriangle\text{-}(CH\text{◐})_w\text{-}(CH\text{◑})_x\text{-}(CH\text{◒})_y\text{-}(CH\text{◓})_z\text{-}CO\text{-}\blacktriangledown]$$ (Structure 3)

wherein:

each of w, x, y, and z are independently 0 or 1, with the proviso that the sum of w + x + y + z is greater than or equal to 1;

each ▲ is independently H, H_2, alkyl, alkoxy, alkyl carboxy, alkyl carboxamide, alkyl amino, alkyl sulfate, aryl, aryl carboxy, aryl carboxamide, aryl amino, aryl sulfate, or is absent;

each of ♤, ♤, ♤, ♤, and ♤ is independently present or absent, and if present designates a terminus of a cyclic group as follows:

♤ designates the N in N▲♤ as a terminus;

♤ designates the C in $(CH◐♤)_w$ as a terminus;

♤ designates the C in $(CH◑♤)_x$ as a terminus;

♤ designates the C in $(CH◒♤)_y$ as a terminus; and

♤ designates the C in $(CH◓♤)_z$ as a terminus;

with the proviso that each Structure 3 independently contains zero, one or two cyclic groups, the termini of each cyclic group being selected from:

♤ as a first terminus and ♤, ♤, ♤, or ♤ as a second terminus;

♤ as a first terminus and ♤, ♤, or ♤ as a second terminus;

♤ as a first terminus and ♤ or ♤ as a second terminus; or

♤ as a first terminus and ♤ as a second terminus;

with the further proviso that:

if ♤ is present, then ◐ is absent;

if ♤ is present, then ◑ is absent;

if ♤ is present, then ◒ is absent;

if ♤ is present, then ◓ is absent;

each cyclic group that is present in Structure 3 further comprises, in addition to its respective termini, a middle section between the termini, Y; and each Y is independently alkyl, alkoxy, alkyl carboxy, alkyl carboxamide, alkyl amino, or alkyl sulfate;

each of ◐, ◑, ◒, and ◓ are independently present or absent, and if present are H, OH, alkyl, alkyl carboxy, alkyl carboxamide, alkyl amino, alkoxy, thioalkyl, alkylthioalkyl, aryl, or heteroaryl;

each of ◐, ◑, ◒, and ◓ are, where present, optionally bonded to a functional end group X, with or without an intervening spacer group ---;

each ▼ is independently OH, alkyl, alkoxy, alkyl carboxy, alkyl carboxamide, alkyl amino, alkyl sulfate, aryl, aryl carboxy, aryl carboxamide, aryl amino, aryl sulfate, or is absent;

with the proviso that homo-bivalent linker compound contains a total of only two functional end groups X, in keeping with the compound being a homo-bivalent linker compound; and

Structure 2 optionally comprises at least one amide bond that is optionally formed from the linkage of two amino acids.

~~28.~~8. The homo-bivalent linker compound of claim ~~27~~7, wherein X is maleimide, azide, alkyne, activated carboxyl or amine.

~~29.~~9. The homo-bivalent linker compound of claim ~~27~~ 7 or ~~28~~8, wherein each spacer group --- is, independently, alkyl, alkoxy, cyclyl, heterocyclyl, aryl, heteroaryl, or substituted versions thereof; optionally, wherein each spacer group --- is, independently, C1-10 alkyl, C1-10 alkoxy, 5-10 membered aryl, 5-10 membered heteroaryl, 5-10 membered heterocyclyl, (C1-10 alkyl)-(5-10 membered aryl), (C1-10 alkyl)-(5-10 membered heteroaryl), or (C1-10 alkyl)-(5-10 membered heterocyclyl); or optionally, wherein each spacer group --- is, independently, C2 to C6 alkyl, ethylene glycol, triethylene glycol, or 1,4-phenylene.

~~30. The homo-bivalent linker compound of claim 29, wherein each spacer group --- is, independently, C1-10 alkyl, C1-10 alkoxy, 5-10 membered aryl, 5-10 membered heteroaryl, 5-10 membered heterocyclyl, (C1-10 alkyl)-(5-10 membered aryl), (C1-10 alkyl)-(5-10 membered heteroaryl), or (C1-10 alkyl)-(5-10 membered heterocyclyl).~~

~~31. The homo-bivalent linker compound of claim 30, wherein each spacer group ~~ ~~is, independently, C2 to C6 alkyl, ethylene glycol, triethylene glycol, or 1,4-phenylene~~.

~~32.~~10. The homo-bivalent linker compound of any of claims ~~27~~ 7 to ~~31~~9, wherein at least one amide bond is a eupeptide bond. an isopeptide bond, or formed from the joining of two amino acids.

~~33. The homo-bivalent linker compound of any of claims 27 to 31, wherein at least one amide bond is an isopeptide bond.~~

~~34. The homo-bivalent linker compound of any of claims 27 to 33, wherein at least one amide bond is formed from the joining of two amino acids.~~

~~35.~~11. The homo-bivalent linker compound of claim ~~34~~10, wherein each of the amino acids is independently naturally occurring or non-naturally occurring; optionally, wherein each of the amino acids is independently an alpha, beta, gamma, or delta amino acid.

~~36. The homo-bivalent linker compound of claim 34, wherein each of the amino acids is independently an alpha, beta, gamma, or delta amino acid.~~

~~37.~~12. The homo-bivalent linker compound of claim ~~34~~10, wherein at least one of the amino acids is an alpha amino acid or a proteogenic amino acid; or wherein each of the amino acids is an alpha amino acid or a proteogenic amino acid.

~~38. The homo-bivalent linker compound of claim 34, wherein at least one of the amino acids is a proteogenic amino acid; or wherein each of the amino acids is a proteogenic amino acid.~~

~~39. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Glycine, wherein:~~

~~with respect to Structure 2:~~

~~each of the spacer groups ~~ ~~are present;~~

~~R and R' are absent;~~

~~a and b are 1;~~

~~c and d are 0;~~

~~with respect to element A, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

~~▲ is H;~~

◐ is H;

⏢ and ⏢ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

⏢ and ⏢ are absent; and

▼ is absent;

with the result that the homo-bivalent linker compound comprises Structure 4:

X---NH-(CH_2)-CO-NH-(CH_2)-CO---X (Structure 4).

40. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Alanine, wherein:

with respect to Structure 2:

each of the spacer groups <---> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

⏢ and ⏢ are absent; and

▼ is absent;

with respect to element B, Structure 3:

~~w is 1;~~

~~x, y, and z are 0;~~

~~▲ is H;~~

~~◐ is methyl;~~

~~⏢ and ⏢ are absent; and~~

~~▼ is absent;~~

~~with the result that the homo-bivalent linker compound comprises Structure 5:~~

~~X---NH-(CH_2)-CO-NH-(CHMethyl)-CO---X (Structure 5).~~

~~41. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Proline, wherein:~~

~~with respect to Structure 2:~~

~~each of the spacer groups <—> are present R and R' are absent;~~

~~a and b are 1;~~

~~c and d are 0;~~

~~with respect to element A, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

~~▲ is H;~~

~~◐ is H;~~

~~⏢ and ⏢ are absent; and~~

~~▼ is absent;~~

~~with respect to element B, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

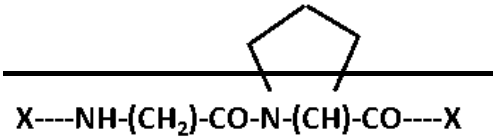
~~▲ is absent;~~

~~⏢ and ⏢ are present;~~

~~Y is propyl and the cyclic group is pyrrolidine; and~~

◐, ◑, and ▼ are absent;

with the result that the homo-bivalent linker compound comprises Structure 6:



(Structure 6).

42. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Valine, wherein:

with respect to Structure 2:

each of the spacer groups <---> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

⏢ and ⏢ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is isopropyl;

⏢ and ⏢ are absent; and

▼ is absent;

with the result that the homo-bivalent linker compound comprises Structure 7:

~~X---NH-(CH_2)-CO-NH-(CH-isopropyl)-CO---X-- (Structure 7).~~

~~43. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Lysine, wherein:~~

~~with respect to Structure 2:~~

~~each of the spacer groups <---> are present R and R' are absent;~~

~~a and b are 1;~~

~~c and d are 0;~~

~~with respect to element A, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

~~▲ is H;~~

~~◐ is H;~~

~~⛢ and ⛢ are absent; and~~

~~▼ is absent;~~

~~with respect to element B, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

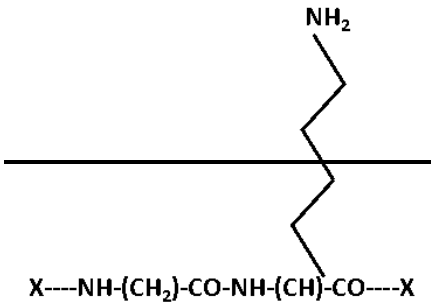
~~▲ is H;~~

~~◐ is butylamino;~~

~~⛢ and ⛢ are absent; and~~

~~▼ is absent;~~

with the result that the homo-bivalent linker compound comprises Structure 8:



(Structure 8).

44. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Lysine, wherein:

with respect to Structure 2:

each of the spacer groups <---> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

♺ and ♺ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

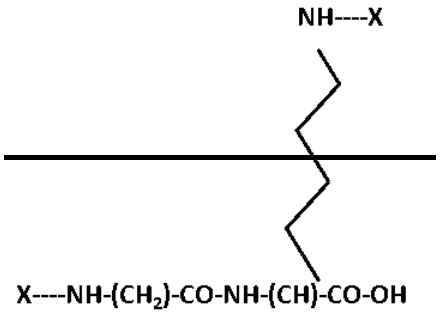
▲ is H;

◐ is butylamino bonded to an X;

♺ and ♺ are absent; and

▼ is OH;

with the result that the bivalent linker compound comprises Structure 9:



(Structure 9).

45. The homo-bivalent linker compound of any of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Aspartic Acid, wherein:

with respect to Structure 2:

each of the spacer groups <—> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

♲ and ♲ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

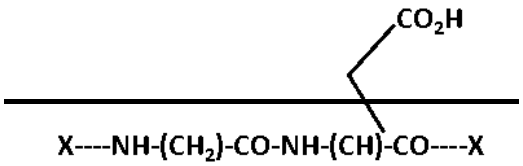
▲ is H;

◐ is acetate;

♲ and ♲ are absent; and

▼ is absent;

with the result that the homo-bivalent linker compound comprises Structure 10:



(Structure 10).

46. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond and an isopeptide bond formed by the joining of Glycine, Aspartic Acid, and Lysine, wherein:

with respect to Structure 2:

each of the spacer groups <—> are present R and R' are absent;

a, b, and c are 1;

d is 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

♺ and ♺ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is acetyl;

♺ and ♺ are absent; and

▼ is OH;

with respect to element C, Structure 3:

w is 1;

x, y, and z are 0;

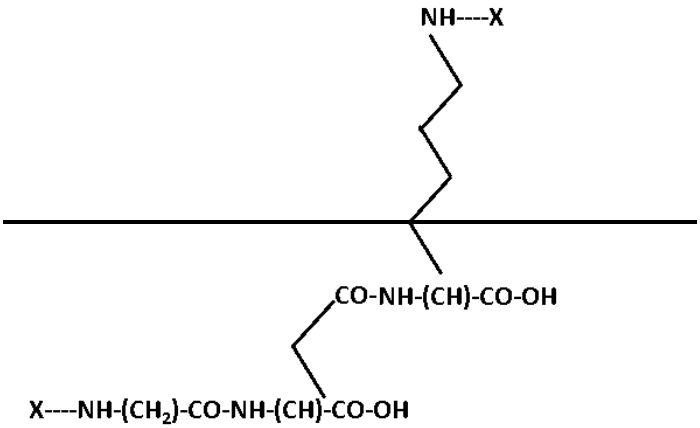
▲ is H;

◐ is butylamino bonded to an X;

♲ and ♲ are absent; and

▼ is OH;

with the result that the homo-bivalent linker compound comprises Structure 11:



(Structure 11).

47. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by the joining of Glycine to Beta-Alanine, wherein:

with respect to Structure 2:

each of the spacer groups <---> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is H;

⛢ and ⛢ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x is 1;

y and z are 0;

▲ is H;

◐ is H;

◑ is H;

⛢, ⛢, and ⛢ are absent; and

▼ is absent;

with the result that the homo-bivalent linker compound comprises Structure 12:

X---NH-(CH_2)-CO-NH-(CH_2)-(CH_2)-CO---X (Structure 12).

48. The homo-bivalent linker compound of claim 27, wherein the compound comprises a cupeptide bond formed by the joining of Valine to Citrulline, wherein:

with respect to Structure 2:

each of the spacer groups <—> are present R and R' are absent;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

▲ is H;

◐ is isopropyl;

⛢ and ⛢ are absent; and

▼ is absent;

with respect to element B, Structure 3:

w is 1;

x, y, and z are 0;

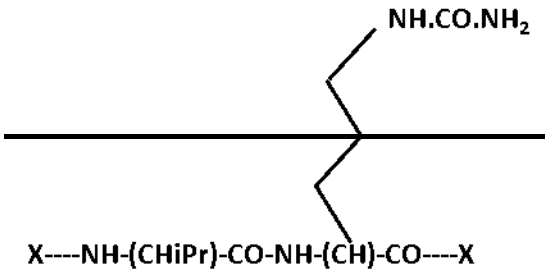
▲ is H;

◐ is propylcarbamoylamino;

♲ and ♲ are absent; and

▼ is absent;

with the result that the homo-bivalent linker compound comprises Structure 13:



(Structure 13).

49. The homo-bivalent linker compound of claim 27, wherein the compound comprises a eupeptide bond formed by joining Lysine to Lysine, wherein:

with respect to Structure 2:

each of the spacer groups <---> are present R is H;

R' is OH;

a and b are 1;

c and d are 0;

with respect to element A, Structure 3:

w is 1;

x, y, and z are 0;

~~▲ is H;~~

~~◐ is butylamino bonded to an X;~~

~~and are absent; and~~

~~▼ is absent;~~

~~with respect to element B, Structure 3:~~

~~w is 1;~~

~~x, y, and z are 0;~~

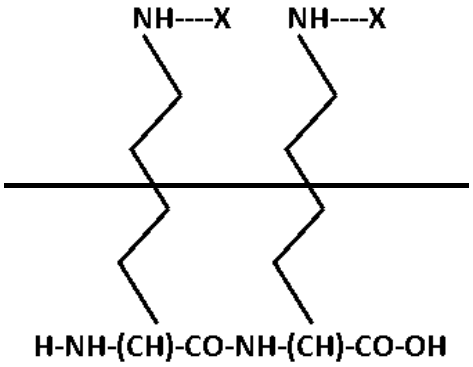
~~▲ is H;~~

~~◐ is butylamino bonded to an X;~~

~~and are absent; and~~

~~▼ is absent;~~

~~with the result that the bivalent linker compound comprises Structure 14:~~



~~(Structure 14).~~

~~50. A branched linker compound of Structure 15:~~

~~L1 (Structure 15)~~
~~|~~
~~L2—B~~
~~|~~
~~L3~~

~~wherein:~~

~~B is a trivalent moiety;~~

~~each of L1, L2 and L3 is a branch group; and~~

~~at least one of L1, L2 and L3 is formed by the joining of B to a homo-bivalent linker compound of any of claims 1 to 49; optionally at least two of L1, L2 and L3 are, independently, formed by the joining of B to a homo-bivalent linker compound of any of claims 1 to 49; optionally each of L1, L2 and L3 are, independently, formed by the joining of B to a homo-bivalent linker compound of any of claims 1 to 49.~~

~~51. The linker compound of any of claims 1-50, wherein the compound is at least 75, 80, 85, 90, 95, 96, 97, 98, 99, or 100% pure.~~

~~52. The linker compound of any of claims 1-50, wherein the compound is about 85-95% pure.~~

~~53. The linker compound of any of claims 1-50, wherein the compound is greater than or equal to 75% pure; greater than or equal to 85% pure; or greater than or equal to 95% pure.~~

~~54.~~13. A multi-conjugate comprising two or more biological moieties joined together by covalent bonds, wherein at least one covalent bond within the multi-conjugate is formed by reaction with a linker compound of any of claims 1 to ~~50~~12; optionally, wherein each of the biological moieties is joined to another biological moiety by a linker compound of any of claims 1 to 12.

~~55. The multi-conjugate of claim 54, wherein each of the biological moieties is joined to another biological moiety by a linker compound of any of claims 1 to 50.~~

~~56.~~14. The multi-conjugate of claim ~~54~~ 13~~or 55~~, wherein the multi-conjugate comprises two, three, four, five, or six biological moieties.

~~57.~~15. The multi-conjugate of ~~any of~~ claim~~s~~ ~~54~~ 13 or~~to~~ 14~~56~~, wherein each biological moiety is, independently, a nucleic acid, peptide, protein, lipid, carbohydrate, carboxylic acid, vitamin, steroid, lignin, small molecule, organometallic compound, or a derivative of any of the foregoing.

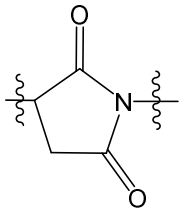
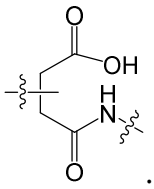
~~58.~~16. The multi-conjugate of any of claims ~~54~~ 13 to ~~57~~15, wherein at least two biological moieties are oligonucleotides; optionally the at least two oligonucleotides are adjacent one another in the multi-conjugate; and optionally each of the oligonucleotides is 15-30, 17-27, 19-26, or 20-25 nucleotides in length.

~~59.~~17. The multi-conjugate of any of claims ~~54~~ 13 to ~~58~~16, wherein at least one of the biological moieties is a double-stranded RNA; optionally an siRNA, a saRNA, or a miRNA; optionally, wherein each of the biological moieties is a double-stranded siRNA.

~~60.~~18. The multi-conjugate of any of claims ~~54~~ 13 to ~~59~~17, wherein at least one of the biological moieties is a single-stranded RNA, optionally an antisense oligonucleotide.

~~61. The multi-conjugate of claim 59, wherein each of the biological moieties is a double-stranded siRNA.~~

~~62.~~19. The multi-conjugate of any of claims ~~54~~ 13 to ~~60~~18, wherein at least one biological moiety is a protein, a peptide, or a derivative thereof.

~~63.~~20. The multi-conjugate of any of claims ~~54~~ 13 to ~~62~~19, having one or more covalent bonds formed by reaction with a homo-bivalent linker compound having maleimide functional groups, each of which, upon reaction, is independently  or .

~~64. A method for synthesizing a multi-conjugate according to any of claims 54 to 63, comprising the steps of reacting a homo-bivalent linker compound according to any of claims 1 to 50 with a first and a second biological moeity, under reaction conditions that promote the formation of a covalent bond between the first biological moiety and the linker compound and a covalent bond between the second biological moiety and the linker compound.~~

~~65. The method of claim 64, wherein the first biological moiety and the second biological moiety are the same and the coupling of each of the biological moieties to the homo-bivalent linker compound is performed simultaneously.~~

~~66. The method of claim 64, wherein the first biological moiety and the second biological moiety are different and the coupling of each of the biological moieties to the homo-bivalent linker compound is performed sequentially under reaction conditions that substantially favor the formation of an isolatable intermediate comprising the homo-bivalent linker monosubstituted with the first biological moiety and substantially prevent dimerization of the first biological moiety.~~

~~67. The method of claim 66, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out in a dilute solution of the first biological moiety with a stoichiometric excess of the homo-bivalent linker compound.~~

~~68. The method of claim 67, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out with a molar excess of the homo-bivalent linker compound of at least about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, or 100.~~

~~69. The method of claim 67, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out with a molar excess of the homo-bivalent linker compound of about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, or 100.~~

~~70. The method of any of claims 66 to 69, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out in a solution comprising water and a water miscible organic co-solvent.~~

~~71. The method of claim 70, wherein the water miscible organic co-solvent comprises DMF, NMP, DMSO, alcohol, or acetonitrile.~~

~~72. The method of claim 70 or 71, wherein the water miscible organic co-solvent comprises about 10, 15, 20, 25, 30, 40, or 50 % (v/v) of the solution.~~

~~73. The method of any of claims 70 to 72, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out at a pH of below about 7, 6, 5, or 4.~~

~~74. The method of any of claims 70 to 72, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out at a pH of about 7, 6, 5, or 4.~~

~~75. The method of any of claims 66 to 69, wherein the coupling of the homo-bivalent linker compound to the first biological moiety is carried out in a solution comprising an anhydrous organic solvent.~~

~~76. The method of claim 75, wherein the anhydrous organic solvent comprises dichloromethane, DMF, DMSO, THF, dioxane, pyridine, alcohol, or acetonitrile.~~

~~77. The method of any of claims 64 to 76, wherein the yield of the multi-conjugate is at least 75, 80, 85, 90, 95, 96, 97, 98, 99, or 100 %.~~

~~78. The method of any of claims 64 to 77, wherein the purity of the multi-conjugate is at least 75, at least 75, 80, 85, 90, 95, 96, 97, 98, 99, or 100 %.~~

~~79.~~21. A compound comprising a homo-bivalent linker of any of claims 1 to ~~49~~ 12 substituted on one end by a biological moiety, wherein the other end of the homo-bivalent linker

is unsubstituted, and wherein the compound is at least 75%, 80, 85, 90, 95, 96, 97, 98, 99, or 100 % pure; optionally, the biological moiety is a nucleic acid, peptide, protein, lipid, carbohydrate, carboxylic acid, vitamin, steroid, lignin, small molecule, organometallic compound, or a derivative of any of the foregoing.

~~80. The compound of claim 79, wherein the biological moeity is a nucleic acid, peptide, protein, lipid, carbohydrate, carboxylic acid, vitamin, steroid, lignin, small molecule, organometallic compound, or a derivative of any of the foregoing.~~

~~81.~~22. A pharmaceutical composition comprising the multi-conjugate of any of claims ~~54~~ 13 to ~~63~~20.

~~82. A composition comprising the multi-conjugate of any of claims 54 to 63 for use in the manufacture of a medicament.~~

~~83.~~23. ~~A method for treating a subject in need of treatment to ameliorate, cure, or prevent the onset of a disease or disorder, the method comprising administering to the subject~~ Use of an effective amount of the multi-conjugate of any of claims ~~54~~ 13 to ~~63~~20 for the manufacture of a medicament for treating a subject in need of treatment to ameliorate, cure, or prevent the onset of a disease or disorder.

~~84.~~24. ~~A method for modulating gene expression in a cell, *in vitro* or *in vivo*, the method comprising delivering to the cell~~ Use of an effective amount of a multi-conjugate according to any of claims ~~54~~ 13 to ~~63~~20 for the manufacture of a medicament for modulating gene expression in a cell, wherein the multi-conjugate comprises at least one biological moiety that has the effect of modulating gene expression.

~~85.~~25. The ~~method~~ use of claim ~~84~~24, wherein the at least one biological moiety silences or reduces gene expression; optionally, wherein the at least one biological moiety is siRNA, miRNA, or an antisense oligonucleotide.

~~86.~~26. The ~~method~~ use of claim ~~84~~24, wherein the at least one biological moeity activates or increases gene expression; optionally wherein the at least one biological moiety is saRNA.

~~87.~~27. ~~A method for delivering, *in vitro* or *in vivo*, two or more biological moeities to a cell per internalization event, comprising administering to the cell~~ Use of a multi-conjugate according to any of claims ~~54~~ 13 to ~~63~~20 for the manufacture of a medicament for delivering two or more biological moeities to a cell per internalization event.

~~88. The method of claim 87, wherein the multi-conjugate is formulated in a lipid nanoparticle.~~

~~89. The method of claim 87, wherein the multi-conjugate is packaged in a viral vector.~~

~~90. The method of claim 87, wherein the multi-conjugate comprises a cell- or tissue-targeting ligand.~~

~~91.~~28. The ~~method~~ use of any of claims ~~83~~23-~~90~~27, wherein the multi-conjugate comprises 3 or more biological moieties in a predetermined stoichiometric ratio.

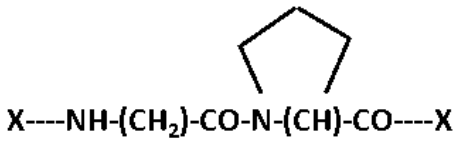
~~92.~~29. ~~A method of treating a disease or condition in a subject comprising the step of administering to the subject~~ Use of an effective amount of a pharmaceutical composition comprising an active pharmaceutical ingredient joined by a covalent bond formed by reaction with a linker compound of any of claims 1 to ~~50~~12 for the manufacture of a medicament for treating a disease or condition in a subject.

~~93.~~30. A homo-bivalent linker compound comprising:

(a) X----NH-(CH_2)-CO-NH-(CH_2)-CO----X (Structure 4);

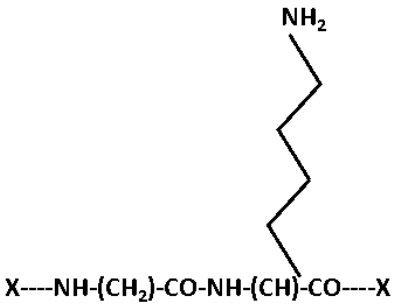
(b) X----NH-(CH_2)-CO-NH-(CHMethyl)-CO----X (Structure 5);

(c)

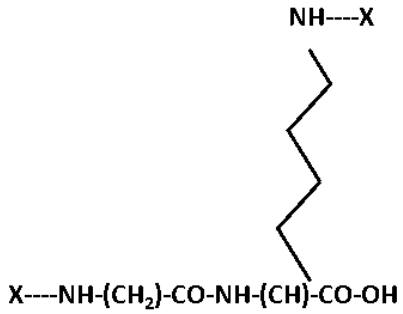


(Structure 6);

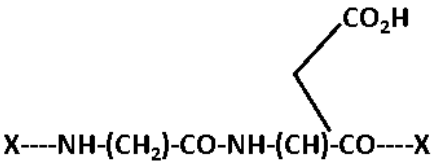
(d) X----NH-(CH_2)-CO-NH-(CH-isopropyl)-CO----X (Structure 7);



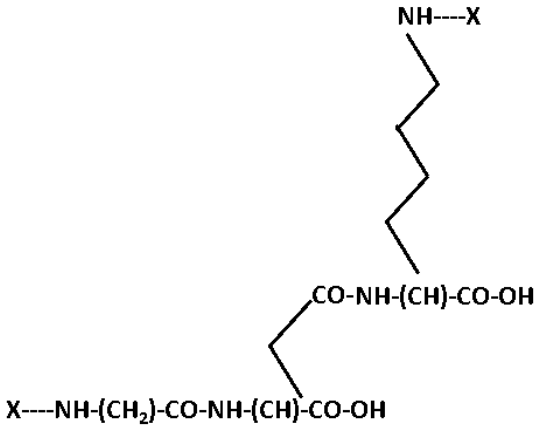
(e) (Structure 8);



(f) (Structure 9);

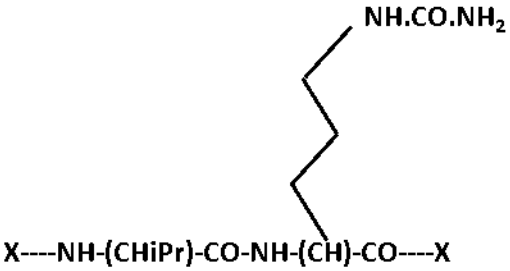


(g) (Structure 10);

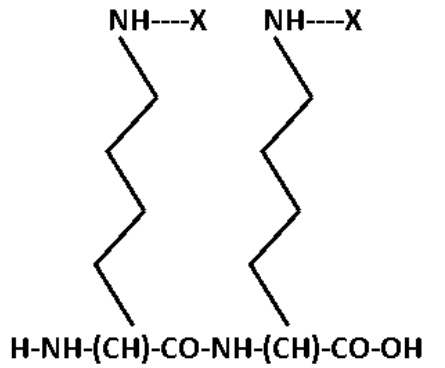


(h) (Structure 11);

(i) X----NH-(CH_2)-CO-NH-(CH_2)-(CH_2)-CO----X (Structure 12);



(j) (Structure 13); or



(k) (Structure 14).

~~94. The method of claim 64, wherein the first and second biological moeity are each independently a nucleic acid, peptide, protein, lipid, carbohydrate, carboxylic acid, vitamin, steroid, lignin, small molecule, organometallic compound, or a derivative of any of the foregoing.~~